What is claimed is:

1. A human IL-18 substitution mutant, wherein said mutant comprises from one to five amino acid substitutions in the sequence of SEQ ID NO:1, said substitutions being at from one to five amino acid residues chosen from the group of: the cysteine at residue 38, the cysteine at residue 68, the cysteine at residue 76, the asparagine at residue 78, the glutamic acid at residue 121, the cysteine at residue 127, the leucine at residue 144, and the aspartic acid at residue 157.

2. The human IL-18 substitution mutant as claimed in Claim 1, wherein said mutant contains a serine in place of cysteine at residue 38 (SEQ ID NO:4).

3. The human IL-18 substitution mutant as claimed in Claim 1, wherein said mutant contains a serine in place of cysteine at residue 38, an aspartic acid in place of cysteine at residue 68, and a cysteine in place of asparagine at residue 78 (SEQ ID NO:5).

4. The human IL-18 substitution mutant as claimed in Claim 1, wherein said mutant contains a serine in place of cysteine at residue 38, an aspartic acid in place of cysteine at residue 68, and a cysteine in place of glutamic acid at residue 121 (SEQ ID NO:6).

5. The human IL-18 substitution mutant as claimed in Claim 3, wherein said mutant contains a serine in place of cysteine at residue 38, an aspartic acid in place of cysteine at residue 68, and a cysteine in place of leucine at residue 144 (SEQ ID NO:7).

6. The human IL-18 substitution mutant as claimed in Claim 1, wherein said mutant contains a serine in place of cysteine at residue 38, an aspartic acid in place of cysteine at residue 68, and a cysteine in place of aspartic acid at residue 157 (SEQ ID NO:8).

7. A biologically active composition comprising a polypeptide conjugated to a water-soluble polymer, wherein the polypeptide is human IL-18 (SEQ ID NO:1).

8. The composition as claimed in Claim 7, wherein the conjugation between the polypeptide and the polymer is covalent.

9. A biologically active composition comprising a polypeptide conjugated to a water-soluble polymer, wherein the polypeptide is a human IL-18 substitution mutant chosen from the group of: SEQ ID NO: 4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and SEQ ID NO:10.

10. The composition as claimed in Claim 9, wherein the conjugation between the polypeptide and the polymer is covalent.

11. The composition as claimed in Claim 9, wherein the water-soluble polymer is a member chosen from the group of: polyethylene glycol homopolymers, polyethylene glycol copolymers, polypropylene glycol homopolymers, poly(N-vinylpyrrolidone), poly(vinyl alcohol), poly(ethylene glycol-co-propylene glycol), poly(N-2-(hydroxypropyl)methacrylamide), poly(sialic acid), poly(N-acryloyl morpholine), and dextran.

12. The composition as claimed in Claim 11, wherein the water-soluble polymer is unsubstituted.

13. The composition as claimed in Claim 11, wherein the water-soluble polymer is substituted at one end with an alkyl group.

14. The composition as claimed in Claim 11, wherein the water-soluble polymer is a polyethylene glycol homopolymer.

15. The composition as claimed in Claim 14, wherein the polyethylene glycol homopolymer is monomethoxy-polyethylene glycol.

16. The composition as claimed in Claim 15, wherein the monomethoxy-polyethylene glycol is chosen from the group of linear monomethoxy-polyethylene glycol and branched monomethoxy-polyethylene glycol .

17. The composition as claimed in Claim 16, wherein the polyethylene glycol homopolymer has a molecular weight of from about 20,000 to about 40,000 daltons.

18. The composition as claimed in Claim 17, wherein the polyethylene glycol homopolymer has a molecular weight of about 20,000 daltons.

19. The composition as claimed in Claim 17, wherein the polyethylene glycol homopolymer has a molecular weight of about 30,000 daltons.

20. The composition as claimed in Claim 17, wherein the polyethylene glycol homopolymer has a molecular weight of about 40,000 daltons.

21. The composition as claimed in Claim 17, wherein the composition is PEGylated native human IL-18 (SEQ ID NO:1).

22. The composition as claimed in Claim 21, wherein the native human IL-18 (SEQ ID NO:1) is PEGylated at the cysteine at residue 38 and at the cysteine at residue 68.

23. A method of treating cancer in a patient by administering a therapeutically effective dose of the composition as claimed in Claim 18.

24. The method as claimed in Claim 23, wherein the cancer comprises an immunosensitive tumor chosen from the group of: renal cell carcinoma, myeloma, lymphoma, and melanoma.

25. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:4, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 38.

26. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:5, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 78.

27. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:6, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 121.

28. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:7, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 144.

29. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:8, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 157.

30. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:9, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 144.

31. The composition as claimed in Claim 30, wherein the water-soluble polymer is chosen from the group of: linear polyethylene glycol homopolymer having a molecular weight of from about 20,000 to about 40,000 daltons and branched polyethylene glycol homopolymer having a molecular weight of from about 20,000 to about 40,000 daltons .

32. The composition as claimed in Claim 31, wherein the linear polyethylene glycol homopolymer has a molecular weight of about 20,000 daltons.

33. The composition as claimed in Claim 19, wherein the human IL-18 substitution mutant has the amino acid sequence set forth in SEQ ID NO:10, and wherein the mutant is conjugated to the water-soluble polymer at the cysteine at residue 157.

34. The composition as claimed in Claim 33, wherein the water-soluble polymer is linear polyethylene glycol homopolymer having a molecular weight of from about 20,000 to about 40,000 daltons.

35. The composition as claimed in Claim 34, wherein the linear polyethylene glycol homopolymer has a molecular weight of about 20,000 daltons.

36. A method of preparing a biologically active composition, said method comprising the steps of:

(a) obtaining a human IL-18 polypeptide (SEQ ID NO:1); and

(b) contacting the polypeptide with a functionalized water-soluble polymer.

37. A method of preparing a biologically active composition, said method comprising the steps of:

(a) obtaining a human IL-18 substitution mutant polypeptide selected from the group consisting of: SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and SEQ ID NO:10; and

(b) contacting the polypeptide with a functionalized water-soluble polymer.

38. The method of Claim 37, wherein the functionalized water soluble polymer is a member chosen from the group of: methoxy polyethylene glycol succinimidyl propionate, MW 20,000; methoxy polyethylene glycol succinimidyl propionate, MW 30,000; methoxy polyethylene glycol succinimidyl butanoate, MW 20,000; succinimidyl ester of carboxymethylated methoxy polyethylene glycol, MW 20,000; methoxy polyethylene glycol aldehyde, MW 20,000; methoxy polyethylene glycol aldehyde, MW 30,000; methoxy polyethylene glycol hydrazide, MW 20,000; methoxy polyethylene glycol maleimide, MW 20,000; methoxy polyethylene glycol maleimide, MW 30,000; methoxy polyethylene glycol orthopyridyl disulfide, MW 20,000; methoxy polyethylene glycol orthopyridyl disulfide, MW 30,000; methoxy polyethylene glycol iodoacetamide, MW 20,000; and methoxy polyethylene glycol iodoacetamide, MW 30,000.

39. The product made by the method as claimed in Claim 36.

40. The product made by the method as claimed in Claim 37.

41. A method of improving the pharmacokinetics and pharmacodynamics of human IL-18 (SEQ ID NO:1) comprising the step of conjugating the human IL-18 (SEQ ID NO:1) to a water-soluble polymer.

42. A method of improving the pharmacokinetics and pharmacodynamics of a human IL-18 substitution mutant chosen from the group of: SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and SEQ ID NO:10, said method comprising the step of conjugating the human IL-18 substitution mutant to a water-soluble polymer.

43. The method as claimed in Claim 33, wherein the water-soluble polymer is a polyethylene glycol homopolymer.

44. The method as claimed in Claim 41, wherein the subcutaneous bioavailability is improved.

45. The method as claimed in Claim 42, wherein the subcutaneous bioavailability is improved.

46. The method as claimed in Claim 41, wherein the subcutaneous bioavailability is improved, and binding to IL-18 binding protein (IL-18 BP) is reduced.

47. The method as claimed in Claim 42, wherein the subcutaneous bioavailability is improved, and binding to IL-18BP is reduced.